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Steroidal Sapogenins. LXVIII.

Their Occurrence in *Agave lecheguilla*

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Agave lecheguilla grows thickly over a wide area of southwestern Texas. The leaves contain, on an average, 1% smilagenin (dry basis) as the sole sapogenin constituent. Smilagenin occurs in nature as a water soluble saponin (sapogenin plus several sugars at C 3). It is necessary that the saponin be extracted from the ground leaf with water and then converted to the water insoluble sapogenin by acidic hydrolysis (1).

In recent years some consideration has been given to the possibility of harvesting wild lecheguilla for recovery not only of its stiff fiber for brushes but also of its steroidal sapogenins. Marker et al. (2) reported 0.1% smilagenin in this species. Our previous collections of the plant (7, 8) from various parts of Texas and northern Mexico had shown a content of smilagenin varying from 0 to 1.0%. Since such variations might be due to locality or to time of year or to both, and since a better knowledge of these factors is essential for utilization consideration, a series of 28 collections was made in Brewster County, Texas, at various chosen topographic sites and at various times of the year. In addition, 10 other collections were made at random sites. This article is largely a report on these materials.

Analytical Methods

The detailed procedure has been given in

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⁴At present Intermediates, Inc., Joliet, Illinois, is producing steroid hormone intermediates derived from smilagenin. Mention of this company's name does not imply endorsement of the company or its products by the United States Department of Agriculture.

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previous publications (4, 6). In general, 10.0 g. of finely ground dry sample was refluxed with 1.5 N hydrochloric acid for 5 hours; the solids were filtered, washed with water, and dried. On extraction of the residue with heptane followed by crystallization, the total crude sapogenin could be obtained. Infra-red analysis gave the percent purity and the identity of the sapogenins. Mono- and dihydroxy mixtures were separated by chromatography (9).

Collection Sites

The samples were collected on the Casner ranch, about 20 miles northeast of Alpine, Texas, on United States Highway 67. Several years ago, the entire ranch was heavily grazed, and the lecheguilla, which is not very palatable, has increased so abundantly that it now controls most of the hilltops and upper slopes of the rolling topography. It develops numerous rhizomes and soon forms clumps 5 to 10 feet across. It normally requires 8 to 10 years for plants to reach maturity, and then the parent plant dies after it produces its fruit. However, there are always plenty of surviving younger plants remaining in the clump. After a reconnaissance of the entire ranch, it was decided to take samples throughout the year from the various slopes of the hills on both sides of the highway. Ten other samples were collected from various ranches throughout the Trans-Pecos region of Texas.

Results

The data from the site series are given in Table I. The analyses of the other collections are not tabulated but will be mentioned at appropriate places in discussing the data in Table I. The following general conclusions are offered.

1. There was great variation in the genin content within a group of comparable collections. With this in mind, there appear to be no differences due to site.

2. The plants from most of the sites had a peak of genin content in September and October, but those from site 4 seem to be an exception.

3. Dead leaves had about the same genin content as green.

4. Roots had the same amount as leaves.

5. Flower stalks were relatively worthless. Of 7 collections, 3 had no genin, 4 had 0.2, 0.6, 0.7, and 0.2%. It was smilagenin in all cases.

6. Two samples of inflorescent buds contained 0.9 and 1.1% of smilagenin.

7. One sample of green fruiting body had 3.7% of hecogenin; 1 of seed, 1.5% total genin, of which 70% was hecogenin and 30% was manogenin; the seed capsule had 2.4% total, of which 70% was hecogenin and 30% was smilagenin.

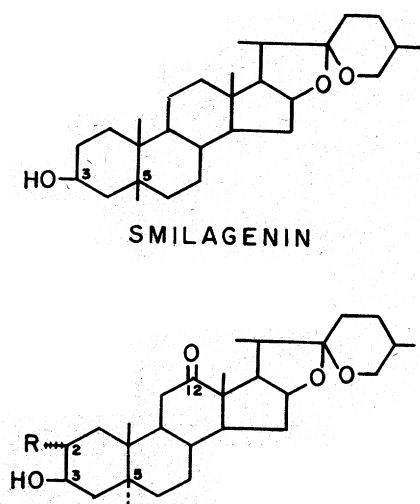
8. The content of genin in leaves averaged about 1.0%. Four other collections of green leaves and 1 of dead averaged 0.9%.

9. Two samples of "cajolla", or the "heart" of the plants, contained 1.6% and 2.0% of smilagenin.

TABLE I
SAPOGENINS IN PLANTS COLLECTED AT DIFFERENT SITES AT DIFFERENT TIMES OF THE YEAR

No.	Date collected	green	Leaves dead	Roots
SITE 1, NORTH SLOPE				
5932	5/56	0.2, sm 100 ¹	0.14, sm 100	
5933	5/56	.4, sm 94	.8, sm 85	0.7, sm 100
6090	9/56	2.3, sm 100	2.2, sm 100	.5, sm 100
6133	10/56	1.1, sm 95	1.1, sm 100	1.3, sm 80; g 20
6207	2/57	.8, sm 100	.5, sm 100	.3, sm 30; g 70
Ave.		1.0	1.0	.7
SITE 2, SOUTH SLOPE				
5935	5/56	0.5, sm 100	1.0, sm 100	
5936	5/56		1.2, sm 100	0.8 sm 100
5937	5/56			
5991	6/56	1.3, sm 100	1.2, sm 100	1.7, sm 100
6091	9/56	1.3, sm 100	1.3, sm 100	1.3, sm 75
6134	10/56	1.5, sm 100	1.0, sm 100	2.6, sm 90
6208	2/57	1.3, sm 100	.8, sm 100	.4, sm 55; g 45
Ave.		1.2	1.1	1.4
SITE 6, SOUTH SLOPE				
5941	5/56	0.9, sm 100	1.2, sm 100	
6095	9/56	.1, sm 100	2.0, sm 100	1.8, sm 95; g 5
6138	10/56	.8, sm 100	1.1, sm 100	1.8, sm 60; g 40
6212	2/57	.8, sm 100	1.1, sm 95	.8, sm 75; g 25
Ave.		.7	1.4	1.4
SITE 3, EAST SLOPE				
5938	5/56	0.3, sm 100	1.5, sm 100	
6092	9/56	1.1, sm 100	1.8, sm 100	0.3, sm 100
6135	10/56	.9 sm 100	1.4, sm 100	2.1, sm 70; g 30
6209	2/57	1.0, sh 100	1.2, sm 95	.9, sm 80; g 20
Ave.		.8	1.5	1.1
SITE 4, WEST SLOPE				
5939	5/56	0.5, sm 100	1.0, sm 100	
6093	9/56	1.5, sm 100	.7, sm 100	0.4, sm 100
6136	10/56	.9, sm 100	.8, sm 100	.6, sm 40; g 60
6210	2/57	1.2, sm 100	.6, sm 100	2.1, sm 90; g 10
Ave.		1.0	.8	1.0
SITE 5, TOP OF HILLS				
5940	5/56	1.3, sm 100	1.0, sm 100	
6094	9/56	1.0, sm 100	1.0, sm 100	2.3, sm 85; g 15
6137	10/56	.8, sm 100	1.3, sm 100	2.2, sm 70; g 30
6211	2/57	1.2, sm 100	1.2, sm 100	1.0, sm 75; g 25
Ave.		1.1	1.1	1.8
OVER-ALL AVE.		1.0	1.1	1.2

¹ The first value is the per cent of genin on a dry matter basis; the last value is the per cent of the individual genin in the total genin. Sm is smilagenin; g is gitogenin.



SMILAGENIN

GITOGENIN, R = OH, 12 DESOXY
 MANOGENIN, R = OH
 HECOGENIN, R = H

Fig. 1. Structures of smilagenin, gitogenin, manigenin, and hecogenin.

10. The steroidal sapogenin in the leaves was always smilagenin. In a few cases the infra-red curves indicated a trace of something else, but this was not identified. The genin in the root was mainly smilagenin, but gitogenin also appeared. The seed had predominantly hecogenin. The formulae for the sapogenins isolated from *Agave lecheguilla* are shown in Figure 1. All have the same spiroketal side chain, but smilagenin differs considerably from the others in that it has a 5β rather than a 5α ring A/B fusion, and it is oxygenated only at C 3. Hecogenin, manogenin, and gitogenin are closely related, and it is possible to conceive of their interconversion by familiar biogenetic principles. This distribution is similar to that in *Yucca brevifolia* (10), where different genins were found in different parts of the plant with a concentration in the seed.

Thus, from the analysis of 38 collections, it can be concluded that the leaves, green or dead, would yield about 1.0% of smilagenin on the dry basis. If it were desired to harvest the roots also as an eradication measure, they, too, would yield 1.0%; but some 20% of this

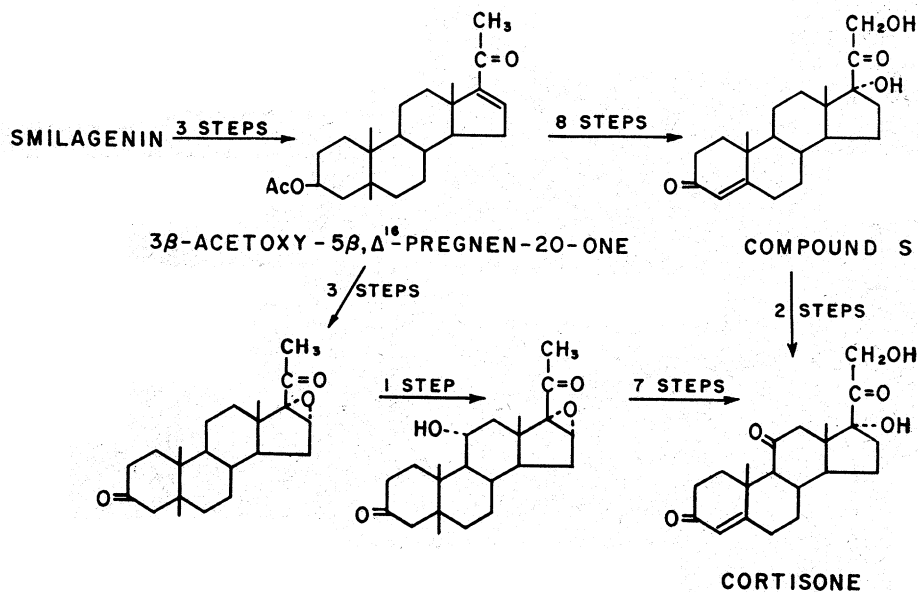


Figure 2. Chemical routes from smilagenin to cortisone.

would be gitogenin. The time of year might have a minor effect on yield. This species is typical of agaves and yuccas in that it contains more genin in the seeds than in any other part of the plant (5). In the seeds, the genin is mostly hecogenin.

Discussion

Smilagenin has no uses per se. However, it is readily converted to 3β -acetoxy- 5β , Δ^{16} -pregnen-20-one (Figure 2). This key intermediate can be converted to compound S and thence by microbiological hydroxylation to cortisone. An alternative route involving microbial hydroxylation of 16α , 17α -oxido- 5β -pregnane-3, 20-dione to the corresponding 11α -hydroxy analogue and then to cortisone has been developed at the Eastern Regional Research Laboratory (3).

At present, the commercial production of bulk cortical hormones or their intermediates is most competitive. Diosgenin from various species of *Dioscorea*, hecogenin from sisal, and sitosterol from crude vegetable oils are all used as starting materials. In most cases, they are captive chemicals, i.e. pharmaceutical companies involved in the production of steroid hormones control sources of the simple starting materials and use these to elaborate the useful pharmaceutical products. Successful utilization of smilagenin from *Agave lecheguilla* would probably require similar handling.⁴

Summary

The leaves of *Agave lecheguilla*, both green and dead, contained about 1.0% smilagenin, dry matter basis. The roots contained about 1.0% total genin, of which about 80% was smilagenin and the rest gitogenin. The seeds contained 1.5 to 2% hecogenin with some manogenin. Topographic sites in Brewster County, Texas, did not affect the genin content, which tended to be higher in September and October. Reactions are shown whereby smilagenin can be converted to cortisone by two different routes.

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